FILE 'HOME' ENTERED AT 10:15:37 ON 08 NOV 2002

=> file medline caplus biosis embase scisearch agricola
COST IN U.S. DOLLARS SINCE FILE ENTRY 0.21 TOTAL SESSION 0.21
FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 10:16:01 ON 08 NOV 2002

FILE 'CAPLUS' ENTERED AT 10:16:01 ON 08 NOV 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE 'BIOSIS' ENTERED AT 10:16:01 ON 08 NOV 2002

FILE 'EMBASE' ENTERED AT 10:16:01 ON 08 NOV 2002

FILE 'SCISEARCH' ENTERED AT 10:16:01 ON 08 NOV 2002

FILE 'AGRICOLA' ENTERED AT 10:16:01 ON 08 NOV 2002

=> s recombinant gelatin
L1 16 RECOMBINANT GELATIN

=> s recombinant (p) gelatin
L2 1022 RECOMBINANT (P) GELATIN

=> s (l1 or l2) (p) human
L3 595 (L1 OR L2) (P) HUMAN

=> s recombinant human gelatin
4 FILES SEARCHED...
L4 1 RECOMBINANT HUMAN GELATIN

=> d l4 1 ibib abs

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:237048 CAPLUS
DOCUMENT NUMBER: 110:237048
TITLE: In vivo effects of recombinant interferon alpha A/D incorporated in gelatin microspheres on murine tumor cell growth
AUTHOR(S): Tabata, Yasuhiko; Uno, Kazuko; Muramatsu, Shigeru; Ikada, Yoshito
CORPORATE SOURCE: Res. Cent. Med. Polym. Biomater., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Japanese Journal of Cancer Research (1989), 80(4), 387-93
CODEN: JJCREP; ISSN: 0910-5050
DOCUMENT TYPE: Journal
LANGUAGE: English
AB I.p. injections of gelatin microspheres contg. a very small amt. of recombinant human interferon .alpha. A/D (A/D-IFN) (IFN-microspheres) plus free A/D-IFN improved the survival of mice bearing ascitic Meth A-R1 cells isolated as IFN-resistant cells under in vitro conditions. The dose of free A/D-IFN in one injection was 10,000 IU, which was insufficient by itself for manifesting in vivo antitumor activity. In these mice, in vivo R1 cell growth was suppressed and macrophage recruitment was enhanced in comparison with mice receiving other control agents. Administration of IFN-microspheres alone was also effective but less than that of IFN-microspheres plus free A/D-IFN. Peritoneal macrophages obtained from normal or R1-bearing mice receiving i.p. injection of IFN-microspheres with or without free A/D-IFN were activated to inhibit the in vitro growth of R1 cells. The intratumoral injection of IFN-microspheres strongly inhibited the growth of solid R1 tumors. I.v. injection of IFN-microspheres was effective in preventing the pulmonary metastasis of

B16 melanoma cells. Thus, the IFN-microsphere is much more effective against tumors than free A[redacted]IFN.

=> d his

(FILE 'HOME' ENTERED AT 10:15:37 ON 08 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 10:16:01 ON 08 NOV 2002

```
L1           16 S RECOMBINANT GELATIN
L2         1022 S RECOMBINANT (P) GELATIN
L3          595 S (L1 OR L2 ) (P) HUMAN
L4            1 S RECOMBINANT HUMAN GELATIN

=> s human gelatin
   5 FILES SEARCHED...
L5           69 HUMAN GELATIN

=> s l5 (p) recombinant
L6            3 L5 (P) RECOMBINANT

=> duplicate remove l6
PROCESSING COMPLETED FOR L6
L7            3 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> d l7 1-3 ibib abs

L7   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:360174  CAPLUS
DOCUMENT NUMBER:          134:365701
TITLE:                    Recombinant gelatins derived from type I collagen
                          .alpha.1 chain, and pharmaceutical applications in
                          vaccines thereof
INVENTOR(S):              Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.;
                          Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S):       Fibrogen, Inc., USA
SOURCE:                   PCT Int. Appl., 130 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001034801      A2   20010517       WO 2000-US30843  20001110
     WO 2001034801      A3   20020131
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1232262         A2   20020821       EP 2000-978469   20001110
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:                  US 1999-165114P  P  19991112
                                        US 2000-204437P  P  20000515
                                        WO 2000-US30843  W  20001110
```

AB The present invention relates to vaccines comprising ***recombinant*** gelatin, to methods of producing and using such vaccines, and to vaccination kits. The present invention relates to ***recombinant*** gelatins and compns. thereof, and methods of producing and using the same. ***Human*** ***gelatins*** with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene ***recombinant*** expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the

.alpha. or .beta. subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the ***recombinant*** gelatins. Well-defined, highly homogenous gelatin fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level endotoxin contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these ***recombinant*** gelatins are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the gelatin that can be used for pharmaceutical or industrial applications.

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:360037 CAPLUS
DOCUMENT NUMBER: 134:362228
TITLE: Recombinant gelatins derived from type I collagen .alpha.1 chain, and pharmaceutical and industrial applications thereof
INVENTOR(S): Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.; Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034646	A2	20010517	WO 2000-US30791	20001110
WO 2001034646	A3	20011206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1232181	A2	20020821	EP 2000-978455	20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 1999-165114P P 19991112
US 2000-204437P P 20000515
WO 2000-US30791 W 20001110

AB The present invention relates to ***recombinant*** gelatins and compns. thereof, and methods of producing and using the same. ***Human*** ***gelatins*** with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene ***recombinant*** expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the .alpha. or .beta. subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the ***recombinant*** gelatins. Well-defined, highly homogenous gelatin fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level endotoxin contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these ***recombinant*** gelatins are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the gelatin that can be used for pharmaceutical or industrial applications.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:237048 CAPLUS
DOCUMENT NUMBER: 110:237048
TITLE: In vivo effects of recombinant interferon alpha A/D incorporated in gelatin microspheres on murine tumor cell growth
AUTHOR(S): Tabata, Yasuhiko; Uno, Kazuko; Muramatsu, Shigeru; Ikada, Yoshito

CORPORATE SOURCE: Res. Ce[illegible]. Med. Polym. Biomater., Kyoto Univ., Kyoto, 606, Ja[illegible]n
SOURCE: Japanese Journal of Cancer Research (1989), 80(4), 387-93
CODEN: JJCREP; ISSN: 0910-5050
DOCUMENT TYPE: Journal
LANGUAGE: English
AB I.p. injections of gelatin microspheres contg. a very small amt. of recombinant human interferon .alpha. A/D (A/D-IFN) (IFN-microspheres) plus free A/D-IFN improved the survival of mice bearing ascitic Meth A-R1 cells isolated as IFN-resistant cells under in vitro conditions. The dose of free A/D-IFN in one injection was 10,000 IU, which was insufficient by itself for manifesting in vivo antitumor activity. In these mice, in vivo R1 cell growth was suppressed and macrophage recruitment was enhanced in comparison with mice receiving other control agents. Administration of IFN-microspheres alone was also effective but less than that of IFN-microspheres plus free A/D-IFN. Peritoneal macrophages obtained from normal or R1-bearing mice receiving i.p. injection of IFN-microspheres with or without free A/D-IFN were activated to inhibit the in vitro growth of R1 cells. The intratumoral injection of IFN-microspheres strongly inhibited the growth of solid R1 tumors. I.v. injection of IFN-microspheres was effective in preventing the pulmonary metastasis of B16 melanoma cells. Thus, the IFN-microsphere is much more effective against tumors than free A/D-IFN.

=> d his

(FILE 'HOME' ENTERED AT 10:15:37 ON 08 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 10:16:01 ON 08 NOV 2002
L1 16 S RECOMBINANT GELATIN
L2 1022 S RECOMBINANT (P) GELATIN
L3 595 S (L1 OR L2) (P) HUMAN
L4 1 S RECOMBINANT HUMAN GELATIN
L5 69 S HUMAN GELATIN
L6 3 S L5 (P) RECOMBINANT
L7 3 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

=> s recombinant (A) gelatin
L8 16 RECOMBINANT (A) GELATIN

=> s l8 not l1
L9 0 L8 NOT L1

=> duplicate remove l1
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L1
L10 10 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)

=> d l10 1-10 ibib abs

L10 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:693122 CAPLUS
DOCUMENT NUMBER: 137:237689
TITLE: ***Recombinant*** ***gelatin*** -like proteins for use as plasma expanders
INVENTOR(S): Bouwstra, Jan Bastiaan; Toda, Yuzo
PATENT ASSIGNEE(S): Fuji Photo Film B.V., Neth.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1238675	A1	20020911	EP 2001-200837	20010306

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
WO 2002070000 A1 2002[redacted]12 WO 2002-NL147 2002[redacted]5
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: EP 2001-200837 A 20010306
AB The invention relates to compns. suitable for plasma substitution comprising as a plasma expander a ***recombinant*** ***gelatin*** -like protein. Characteristic is that the gelatin-like protein essentially is free of hydroxyproline. This absence of hydroxyproline prevents the compn. from gelling and thus allows the use of high-mol. wt. proteins in order to establish a suitable colloid osmotic pressure. Specific advantage of the gelatin-like proteins is that these avoid the risk of anaphylactic shock that exists in conjunction with the use of com. available prepns.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:434852 BIOSIS
DOCUMENT NUMBER: PREV200200434852
TITLE: ***Recombinant*** ***gelatin*** and full-length triple helical collagen.
AUTHOR(S): Olsen, David R.; Chang, Robert (1); McMullin, Hugh; Hitzeman, Ronald A.; Chisholm, George
CORPORATE SOURCE: (1) Hillsborough, CA USA
ASSIGNEE: Cohesion Technologies, Inc.; Genotypes, Inc., Pacifica, CA, USA
PATENT INFORMATION: US 6413742 July 02, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (July 2, 2002) Vol. 1260, No. 1, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB Methods are disclosed for simplified recombinant production of fibrillar collagens. DNAs encoding fibrillar collagen monomers lacking the N propeptide, the C propeptide, or both propeptides are introduced into recombinant host cells and expressed. Trimeric collagen is recovered from the recombinant host cells.

L10 ANSWER 3 OF 10 AGRICOLA
ACCESSION NUMBER: 2002:31684 AGRICOLA
DOCUMENT NUMBER: CAT11118434
TITLE: ***Recombinant*** ***gelatin*** and collagen from methylotrophic yeasts.
AUTHOR(S): Bruin, Eric C. de.
AVAILABILITY: DNAL (DISS F2002009)
SOURCE: 2002? 109 p. : ill. ; 24 cm
Publisher: [Wageningen : s.n., 2002?]
ISBN: 905808583X.
NOTE: "Stellingen" inserted.
Thesis (doctoral)--Wageningen Universiteit, 2002.
Includes bibliographical references (p. 95-104).
Voorword and summary in Dutch.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Bibliography; Dissertation; (MONOGRAPH)
FILE SEGMENT: Non-U.S. Imprint other than FAO
LANGUAGE: English
SUMMARY LANGUAGE: Dutch

L10 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:288888 CAPLUS
DOCUMENT NUMBER: 137:5071

TITLE: Endogenous prolyl 4-hydroxylation in Hansenula polymorpha and its use for the production of hydroxylated ***recombinant*** ***gelatin***
AUTHOR(S): De Bruin, Eric C.; Werten, Marc W. T.; Laane, Colja; De Wolf, Frits A.
CORPORATE SOURCE: Agrotechnological Research Institute (ATO B.V.), Wageningen, 6708 PD, Neth.
SOURCE: FEMS Yeast Research (2002), 1(4), 291-298
CODEN: FYREAG; ISSN: 1567-1356
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several yeast systems have recently been developed for the recombinant prodn. of gelatin and collagen. Amino acid sequence-specific prolyl 4-hydroxylation is essential for the gel-forming capacity of gelatin and for the proper folding of (pro)collagen. This post-translational modification is generally considered to be absent in microbial eukaryotic systems and therefore co-expression of heterologous (human or animal) prolyl 4-hydroxylase would be required. However, we found that the well-known protein expression host Hansenula polymorpha unexpectedly does have the endogenous capacity for prolyl 4-hydroxylation. Without co-expression of a heterologous prolyl 4-hydroxylase, both an endogenous collagen-like protein and a heterologously expressed collagen fragment were found to be sequence-specifically hydroxylated.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:360174 CAPLUS
DOCUMENT NUMBER: 134:365701
TITLE: ***Recombinant*** ***gelatins*** derived from type I collagen .alpha.1 chain, and pharmaceutical applications in vaccines thereof
INVENTOR(S): Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.; Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034801	A2	20010517	WO 2000-US30843	20001110
WO 2001034801	A3	20020131		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1232262	A2	20020821	EP 2000-978469	20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 1999-165114P P 19991112
US 2000-204437P P 20000515
WO 2000-US30843 W 20001110

AB The present invention relates to vaccines comprising ***recombinant*** ***gelatin*** , to methods of producing and using such vaccines, and to vaccination kits. The present invention relates to ***recombinant*** ***gelatins*** and compns. thereof, and methods of producing and using the same. Human gelatins with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene recombinant expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the .alpha. or .beta. subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the

recombinant ***gelatins*** . Well-defined, highly homogenous gelatin fragments ranging in size from 6-65 kDa are produced which can support cell attachment activity, have lower level endotoxin contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these ***recombinant*** ***gelatins*** are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the gelatin that can be used for pharmaceutical or industrial applications.

L10 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:360038 CAPLUS
DOCUMENT NUMBER: 134:362258
TITLE: Animal collagens and their use for gelatins preparation in transgenic plants
INVENTOR(S): Bell, Marcum P.; Neff, Thomas B.; Polarek, James W.; Seeley, Todd W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034647	A2	20010517	WO 2000-US30792	20001110
WO 2001034647	A3	20011206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1232182	A2	20020821	EP 2000-978456	20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 1999-439058 A 19991112
WO 2000-US30792 W 20001110

AB The present invention provides animal collagens and gelatins and compns. thereof, and methods of producing the same. Various forms of collagen gene have been cloned and sequenced from bovine and porcine, which include Type I .alpha.1 chain, Type III .alpha.1 chain and Type I .alpha.2 chain. These procollagen genes can be used for to prep. gelatins in transgenic plants by pharmaceutic and industrial applications.

L10 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:360037 CAPLUS
DOCUMENT NUMBER: 134:362228
TITLE: ***Recombinant*** ***gelatins*** derived from type I collagen .alpha.1 chain, and pharmaceutical and industrial applications thereof
INVENTOR(S): Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.; Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034646	A2	20010517	WO 2000-US30791	20001110
WO 2001034646	A3	20011206		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,				

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, [redacted], RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1232181 A2 20020821 EP 2000-978455 20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.: US 1999-165114P P 19991112
US 2000-204437P P 20000515
WO 2000-US30791 W 20001110

AB The present invention relates to ***recombinant*** ***gelatins*** and compns. thereof, and methods of producing and using the same. Human gelatins with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene recombinant expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the .alpha. or .beta. subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the ***recombinant*** ***gelatins*** . Well-defined, highly homogenous gelatin fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level endotoxin contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these ***recombinant*** ***gelatins*** are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the gelatin that can be used for pharmaceutical or industrial applications.

L10 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:441507 CAPLUS
DOCUMENT NUMBER: 133:81505
TITLE: Silver halide photographic emulsion containing ***recombinant*** ***gelatin*** -like protein
INVENTOR(S): De Wolf, Anton; Werten, Marc Willem Theodoor; Wisselink, Hendrik Wouter; Jansen-Van Den Bosch, Tanja Jacoba; Toda, Yuzo; Van Heerde, Georg Valentino; Bouwstra, Jan Bastiaan
PATENT ASSIGNEE(S): Fuji Photo Film B.V., Neth.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1014176	A2	20000628	EP 1999-204382	19991217
EP 1014176	A3	20000802		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6150081	A	20001121	US 1998-219849	19981223

PRIORITY APPLN. INFO.: US 1998-219849 A 19981223
NL 1997-1007908 A 19971224

AB The invention provides a nonnatural gelatin-like protein prepd. by genetic engineering and having a mol. wt. of from about 2500 to about 100,000 and an amino acid sequence comprising more than 4 different amino acids. The invention also provides a tabular silver halide photog. emulsion contg. the gelatin-like protein as a peptizer. Tabular grains account for more than 75% of the total grain-projected area of the photog. emulsion, and the silver halide grains are nucleated in the presence of a nucleation peptizer and thereafter grown in the presence of a growth peptizer, wherein either the nucleation peptizer or the growth peptizer can be the ***recombinant*** ***gelatin*** -like protein.

L10 ANSWER 9 OF 10 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 1999387091 MEDLINE
DOCUMENT NUMBER: 99387091 PubMed ID: 10455232
TITLE: High-yield secretion of ***recombinant***

gelatin by Pichia pastoris.
AUTHOR: Werten M W; [redacted]n den Bosch T J; Wind R D; Mooi[redacted]bek H; de Wolf F A
CORPORATE SOURCE: Agrotechnological Research Institute (ATO-DLO), Bornsesteeg 59, 6708 PD Wageningen, The Netherlands..
m.w.t.werten@ato.dlo.nl
SOURCE: YEAST, (1999 Aug) 15 (11) 1087-96.
Journal code: 8607637. ISSN: 0749-503X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991020

AB Recombinant non-hydroxylated gelatins based on mouse type I and rat type III collagen sequences were secreted from the methylotrophic yeast Pichia pastoris, using the Saccharomyces cerevisiae alpha-mating factor prepro signal. Proteolytic degradation could be minimized to a large extent by performing fermentations at pH 3.0 and by adding casamino acids to the medium, even though gelatin is extremely susceptible to proteolysis due to its open, unfolded structure. Proteolytic cleavage at specific mono-arginylic sites, by a putative Kex2-like protease, could be successfully abolished by site-directed mutagenesis of these sites. Production levels as high as 14.8 g/l clarified both were obtained, using multicopy tranformants. To our knowledge, this represents the highest level of heterologous protein secretion reported to date for P. pastoris.

L10 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:299673 CAPLUS
DOCUMENT NUMBER: 122:89288
TITLE: The use of gelatin as a vehicle for drug and peptide delivery
AUTHOR(S): Di Silvio, L.; Courteney-Harris, R. G.; Downes, S.
CORPORATE SOURCE: Institute Orthopedics, Royal National Orthopedic Hospital Trust, Stanmore, Middlesex, HA7 4LP, UK
SOURCE: Journal of Materials Science: Materials in Medicine (1994), 5(11), 819-23
CODEN: JSMMEL; ISSN: 0957-4530
PUBLISHER: Chapman & Hall
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Gelatin, a naturally occurring polymer, has been investigated as a vehicle for drug delivery in two different delivery systems: microspheres and as a coating on titanium implants. The gelatin was loaded with recombinant human growth hormone (hGH) which was dispersed within the polymer matrix prior to crosslinking; it was then made into microspheres or coated onto the implants. The release of hGH was monitored in vitro using an ELISA system. The effects of pH on the swelling kinetics and the phys. properties of the loaded gelatin in the microsphere system were studied. In addn., the effect of ultrasound on the microspheres was investigated as a possible method for controlling the rate of release of hGH, it was demonstrated that exposure to ultrasound significantly increased hGH release. Biocompatibility of the gelatin was detd. using both primary human (HOB) and rabbit (ROB) osteoblast-like cells in culture.

=> d his

(FILE 'HOME' ENTERED AT 10:15:37 ON 08 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 10:16:01 ON 08 NOV 2002
L1 16 S RECOMBINANT GELATIN
L2 1022 S RECOMBINANT (P) GELATIN
L3 595 S (L1 OR L2) (P) HUMAN
L4 1 S RECOMBINANT HUMAN GELATIN
L5 69 S HUMAN GELATIN
L6 3 S L5 (P) RECOMBINANT
L7 3 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)

```
L8            16 S RECOMBINANT (A) GELATIN
L9             0 S L8 NOT L1
L10           10 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)

=> s l2 (p) homogeneous
L11            0 L2 (P) HOMOGENEOUS

=> s l2 (p) hydroxylat?
L12           20 L2 (P) HYDROXYLAT?

=> duplicate remove l12
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L12
L13            6 DUPLICATE REMOVE L12 (14 DUPLICATES REMOVED)

=> d l13 1-6 ibib abs

L13  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2002 ACS         DUPLICATE 1
ACCESSION NUMBER:         2002:288888  CAPLUS
DOCUMENT NUMBER:          137:5071
TITLE:                    Endogenous prolyl 4-  ***hydroxylation***  in
                          Hansenula polymorpha and its use for the production of
                            ***hydroxylated***     ***recombinant***
                            ***gelatin***
AUTHOR(S):                De Bruin, Eric C.; Werten, Marc W. T.; Laane, Colja;
                          De Wolf, Frits A.
CORPORATE SOURCE:         Agrotechnological Research Institute (ATO B.V.),
                          Wageningen, 6708 PD, Neth.
SOURCE:                   FEMS Yeast Research (2002), 1(4), 291-298
                          CODEN: FYREAG; ISSN: 1567-1356
PUBLISHER:                Elsevier Science B.V.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Several yeast systems have recently been developed for the
       ***recombinant***  prodn. of  ***gelatin***  and collagen.  Amino acid
     sequence-specific prolyl 4-  ***hydroxylation***  is essential for the
     gel-forming capacity of  ***gelatin***  and for the proper folding of
     (pro)collagen.  This post-translational modification is generally
     considered to be absent in microbial eukaryotic systems and therefore
     co-expression of heterologous (human or animal) prolyl 4-hydroxylase would
     be required.  However, we found that the well-known protein expression
     host Hansenula polymorpha unexpectedly does have the endogenous capacity
     for prolyl 4-  ***hydroxylation***  .  Without co-expression of a
     heterologous prolyl 4-hydroxylase, both an endogenous collagen-like
     protein and a heterologously expressed collagen fragment were found to be
     sequence-specifically  ***hydroxylated***  .
REFERENCE COUNT:          35    THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13  ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:360174  CAPLUS
DOCUMENT NUMBER:          134:365701
TITLE:                    Recombinant gelatins derived from type I collagen
                          .alpha.1 chain, and pharmaceutical applications in
                          vaccines thereof
INVENTOR(S):              Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.;
                          Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S):       Fibrogen, Inc., USA
SOURCE:                   PCT Int. Appl., 130 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001034801      A2   20010517       WO 2000-US30843  20001110
     WO 2001034801      A3   20020131
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
```

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1232262 A2 20020821 EP 2000-978469 20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 1999-165114P P 19991112
US 2000-204437P P 20000515
WO 2000-US30843 W 20001110

AB The present invention relates to vaccines comprising recombinant gelatin, to methods of producing and using such vaccines, and to vaccination kits. The present invention relates to recombinant gelatins and compns. thereof, and methods of producing and using the same. Human gelatins with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene recombinant expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the .alpha. or .beta. subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the recombinant gelatins. Well-defined, highly homogenous gelatin fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level endotoxin contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these recombinant gelatins are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the gelatin that can be used for pharmaceutical or industrial applications.

L13 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:360037 CAPLUS
DOCUMENT NUMBER: 134:362228
TITLE: Recombinant gelatins derived from type I collagen .alpha.1 chain, and pharmaceutical and industrial applications thereof
INVENTOR(S): Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.; Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034646	A2	20010517	WO 2000-US30791	20001110
WO 2001034646	A3	20011206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1232181 A2 20020821 EP 2000-978455 20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 1999-165114P P 19991112
US 2000-204437P P 20000515
WO 2000-US30791 W 20001110

AB The present invention relates to recombinant gelatins and compns. thereof, and methods of producing and using the same. Human gelatins with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene recombinant expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is

cloned for the expression in Pichia pastoris which is also transformed with genes for the .alpha. [redacted] .beta. subunit of human prolyl [redacted] 4-hydroxylase, which is used to improve the stability of the recombinant gelatins. Well-defined, highly homogenous gelatin fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level endotoxin contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these recombinant gelatins are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the gelatin that can be used for pharmaceutical or industrial applications.

L13 ANSWER 4 OF 6 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002027572 MEDLINE
DOCUMENT NUMBER: 21370381 PubMed ID: 11477225
TITLE: Secreted production of a custom-designed, highly hydrophilic gelatin in Pichia pastoris.
AUTHOR: Werten M W; Wisselink W H; Jansen-van den Bosch T J; de Bruin E C; de Wolf F A
CORPORATE SOURCE: Agrotechnological Research Institute (ATO BV), Bornsesteeg 59, 6708 PD Wageningen, The Netherlands.. m.w.t.werten@ato.wag-ur.nl
SOURCE: PROTEIN ENGINEERING, (2001 Jun) 14 (6) 447-54. Journal code: 8801484. ISSN: 0269-2139.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020404
Entered Medline: 20020402
AB A custom-designed, highly hydrophilic ***gelatin*** was produced in Pichia pastoris. Secreted production levels in single-copy transformants were in the range 3-6 g/l of clarified broth and purification to near homogeneity could be accomplished by differential ammonium sulfate precipitation. Despite the fact that ***gelatins*** are highly susceptible to proteolysis because of their unfolded structure, the ***recombinant*** protein was shown to be fully intact by SDS-PAGE, N-terminal sequencing, gel filtration chromatography and mass spectrometry. Owing to its highly hydrophilic nature, the migration of the synthetic ***gelatin*** in SDS-PAGE was severely delayed. Esterification of the carboxylic amino acid side chains resulted in normal migration. The high polarity of the synthetic ***gelatin*** also accounts for its negligible surface activity in water at concentrations up to 5% (w/v), as determined by tensiometry. Circular dichroism spectrometry showed that the non- ***hydroxylated*** ***gelatin*** did not form triple helices at 4 degrees C. The spectrum was even more representative of the random coil conformation than the spectrum of natural non- ***hydroxylated*** ***gelatins*** .

L13 ANSWER 5 OF 6 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999387091 MEDLINE
DOCUMENT NUMBER: 99387091 PubMed ID: 10455232
TITLE: High-yield secretion of recombinant gelatins by Pichia pastoris.
AUTHOR: Werten M W; van den Bosch T J; Wind R D; Mooibroek H; de Wolf F A
CORPORATE SOURCE: Agrotechnological Research Institute (ATO-DLO), Bornsesteeg 59, 6708 PD Wageningen, The Netherlands.. m.w.t.werten@ato.dlo.nl
SOURCE: YEAST, (1999 Aug) 15 (11) 1087-96. Journal code: 8607637. ISSN: 0749-503X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991020
AB ***Recombinant*** non- ***hydroxylated*** ***gelatins*** based

on mouse type I and rat type III collagen sequences were secreted from the methylotrophic yeast Pichia pastoris, using the Saccharomyces cerevisiae alpha-mating factor prepro signal. Proteolytic degradation could be minimized to a large extent by performing fermentations at pH 3.0 and by adding casamino acids to the medium, even though ***gelatin*** is extremely susceptible to proteolysis due to its open, unfolded structure. Proteolytic cleavage at specific mono-arginylic sites, by a putative Kex2-like protease, could be successfully abolished by site-directed mutagenesis of these sites. Production levels as high as 14.8 g/l clarified both were obtained, using multicopy tranformants. To our knowledge, this represents the highest level of heterologous protein secretion reported to date for P. pastoris.

L13 ANSWER 6 OF 6 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 96202043 MEDLINE
DOCUMENT NUMBER: 96202043 PubMed ID: 8620038
TITLE: Comparison of cleavage site specificity of gelatinases A and B using collagenous peptides.
AUTHOR: Xia T; Akers K; Eisen A Z; Seltzer J L
CORPORATE SOURCE: Division of Dermatology, Washington University School of Medicine, St. Louis, MO 63110, USA.
CONTRACT NUMBER: AR07824 (NIAMS)
AR12129 (NIAMS)
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Apr 16) 1293 (2) 259-66.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960627
Last Updated on STN: 20000303
Entered Medline: 19960619

AB The gelatinases (type IV collagenases) are members of the matrix metalloproteinase family that not only have a high degree of structural homology but are known to be nearly identical in their digestion profile against macromolecular substrates. We have shown previously that the preferred cleavage sites in the hydrolysis of type I ***gelatin*** , catalyzed by gelatinase A (72 kDa type IV collagenase), are bracketed by hydroxyproline in the P5 and P5' positions. In this report, a kinetic investigation using a series of collagenous dodecylpeptides in which the P5 and P5' hydroxyprolines were systematically varied and used as substrates for ***recombinant*** human gelatinase A, we show that replacement with either proline or alanine always resulted in increased Km. In contrast, substitution of the ***hydroxylated*** amino acids tyrosine and serine at P5 and P5' reduced the Km significantly, indicating that the hydroxyl moiety of the hydroxyproline is the functional group responsible for favorable enzyme-substrate affinity. This was shown by the kcat/Km ratio, which was doubled by the substitution of serine in that site. Cleavage of the same series of dodecylpeptides by ***recombinant*** human gelatinase B (92 kDa type IV collagenase) showed a very different kinetic profile for which no patterns were discernible. In subsequent comparisons of the two enzymes, it was found that gelatinase B cleaved the thiopeptolide substrate AcProLeuGly-S-LeuGly-OC2H5 at double the velocity of gelatinase A. In contrast, gelatinase A digested type I ***gelatin*** about 2.5-times faster than gelatinase B. SDS-PAGE analysis of ***gelatin*** cleavage products showed different patterns of product peptides for each enzyme. Further comparisons of the proteinases using synthetic peptide substrates with variations in size and in substituents at the P2' site again showed marked kinetic differences. Although these two matrix metalloproteinases seem similar in that they are both gelatinolytic and can degrade a nearly identical battery of macromolecular matrix components including type IV collagen, it is clear from these results that they are very different enzymatically. Since the regulatory portions of gelatinases A and B differ markedly, it has been assumed that the enzymes serve the same function, but respond to different stimuli. The differences in substrate specificity described herein suggest that their proposed physiological roles may require reevaluation.

```
=> d his

     (FILE 'HOME' ENTERED AT 10:15:37 ON 08 NOV 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:16:01 ON 08 NOV 2002
L1           16 S RECOMBINANT GELATIN
L2         1022 S RECOMBINANT (P) GELATIN
L3          595 S (L1 OR L2 ) (P) HUMAN
L4            1 S RECOMBINANT HUMAN GELATIN
L5           69 S HUMAN GELATIN
L6            3 S L5 (P) RECOMBINANT
L7            3 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
L8           16 S RECOMBINANT (A) GELATIN
L9            0 S L8 NOT L1
L10          10 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L11           0 S L2 (P) HOMOGENEOUS
L12          20 S L2 (P) HYDROXYLAT?
L13           6 DUPLICATE REMOVE L12 (14 DUPLICATES REMOVED)

=> duplicate remove l2
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L2
L14          335 DUPLICATE REMOVE L2 (687 DUPLICATES REMOVED)

=> s l14 (p) endotoxin
L15           3 L14 (P) ENDOTOXIN

=> d l15 1-3 ibib abs

L15  ANSWER 1 OF 3     MEDLINE
ACCESSION NUMBER:    97217420     MEDLINE
DOCUMENT NUMBER:     97217420   PubMed ID: 9063441
TITLE:               Production and characterization of recombinant active mouse
                     gelatinase B from eukaryotic cells and in vivo effects
                     after intravenous administration.
AUTHOR:              Masure S; Paemen L; Van Aelst I; Fiten P; Proost P; Billiau
                     A; Van Damme J; Opdenakker G
CORPORATE SOURCE:    Rega Institute for Medical Research, Laboratory of
                     Molecular Immunology, University of Leuven, Belgium.
SOURCE:              EUROPEAN JOURNAL OF BIOCHEMISTRY, (1997 Feb 15) 244 (1)
                     21-30.
                     Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY:        GERMANY: Germany, Federal Republic of
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199704
ENTRY DATE:          Entered STN: 19970422
                     Last Updated on STN: 20000303
                     Entered Medline: 19970407
AB   Gelatinase B is a matrix metalloproteinase involved in tissue remodelling.
     When mouse cells are triggered in vitro with interleukin-1, bacterial
       ***endotoxin***  , virus-mimicking double-stranded RNA or cytokine
     inducers, they produce gelatinase B. To test the effects of gelatinase B
     in vivo, the enzyme was expressed in Chinese hamster ovary (CHO) cells.
     Hybrid genomic DNA-cDNA constructs under the control of two constitutive
     viral promoters were generated by PCR-mediated exon amplification. In
     vitro transcription and translation of the mRNA in reticulocyte lysate
     yielded the correct 79-kDa protein, and expression in CHO cells resulted
     in an intact glycosylated 110-kDa gelatinase B which was enzymically
     active. However, the production yields of   ***recombinant***   enzyme
     from 50 tested clones were low and cell-culture supernatants contained
     significant amounts of copurifiable endogenous CHO gelatinase B.
     Therefore, the enzyme was expressed in the yeast Pichia pastoris.
       ***Recombinant***   proenzyme was secreted and recovered from the yeast
     culture medium at 10 mg/l. Amino-terminal sequence analysis indicated that
     affinity purification of the   ***recombinant***   protein on
       ***gelatin***  -Sepharose yielded the expected N-glycosylated proenzyme
     form (110 kDa) in addition to an amino-terminally truncated unglycosylated
     variant (69 kDa). Both forms had gelatinolytic activity on zymography. The
```

recombinant mouse gelatinase B was used to determine its pharmacokinetics and its hematological effects in vivo. After intravenous injection in rabbits, gelatinase B disappeared from the circulation within 6 h. In addition to a transient leukopenia, we observed a rapid increase in leukocytosis, which indicates that gelatinase B might be a factor involved in the desorption of adherent leukocytes from the vascular bed and in the release of leukocytes from the bone marrow. Gelatinase B secretion and activation might well be one of the crucial molecular mechanisms explaining leukocytosis which is associated with infections and almost all types of inflammation.

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:360174 CAPLUS
DOCUMENT NUMBER: 134:365701
TITLE: Recombinant gelatins derived from type I collagen .alpha.1 chain, and pharmaceutical applications in vaccines thereof
INVENTOR(S): Chang, Robert C.; Kivirikko, Kari I.; Neff, Thomas B.; Olsen, David R.; Polarek, James W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034801	A2	20010517	WO 2000-US30843	20001110
WO 2001034801	A3	20020131		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1232262	A2	20020821	EP 2000-978469	20001110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 1999-165114P P 19991112
US 2000-204437P P 20000515
WO 2000-US30843 W 20001110

AB The present invention relates to vaccines comprising ***recombinant*** ***gelatin*** , to methods of producing and using such vaccines, and to vaccination kits. The present invention relates to ***recombinant*** ***gelatins*** and compns. thereof, and methods of producing and using the same. Human ***gelatins*** with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene ***recombinant*** expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the .alpha. or .beta. subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the ***recombinant*** ***gelatins*** . Well-defined, highly homogenous ***gelatin*** fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level ***endotoxin*** contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these ***recombinant*** ***gelatins*** are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the ***gelatin*** that can be used for pharmaceutical or industrial applications.

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:360037 CAPLUS
DOCUMENT NUMBER: 134:362228
TITLE: Recombinant gelatins derived from type I collagen .alpha.1 chain, and pharmaceutical and industrial applications thereof

INVENTOR(S): Chang, [redacted]bert C.; Kivirikko, Kari I.; Neff, Thomas B.; Olsen, [redacted]vid R.; Polarek, James W.
PATENT ASSIGNEE(S): Fibrogen, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034646	A2	20010517	WO 2000-US30791	20001110
WO 2001034646	A3	20011206		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1232181	A2	20020821	EP 2000-978455	20001110

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 1999-165114P	P	19991112
	US 2000-204437P	P	20000515
	WO 2000-US30791	W	20001110

AB The present invention relates to ***recombinant*** ***gelatins*** and compns. thereof, and methods of producing and using the same. Human ***gelatins*** with discrete fragments of the .alpha.1(I) chain of human type I collagen is produced using a yeast multi-gene ***recombinant*** expression system. Specific fragments of cDNA for .alpha.1(I) chain from human type I collagen is cloned for the expression in Pichia pastoris which is also transformed with genes for the .alpha. or .beta. subunit of human prolyl 4-hydroxylase, which is used to improve the stability of the ***recombinant*** ***gelatins*** . Well-defined, highly homogenous ***gelatin*** fragments ranging in size from 6-65 kDa are produced, which can support cell attachment activity, have lower level ***endotoxin*** contamination, and are proteolytically more stable. The peptide profile of thermal, acid, and enzymic hydrolysis anal., and antigenicity of these ***recombinant*** ***gelatins*** are studied. This presents unsurpassed flexibility in terms of the size and biophys. properties of the ***gelatin*** that can be used for pharmaceutical or industrial applications.

=> d his

(FILE 'HOME' ENTERED AT 10:15:37 ON 08 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 10:16:01 ON 08 NOV 2002

L1	16	S RECOMBINANT GELATIN
L2	1022	S RECOMBINANT (P) GELATIN
L3	595	S (L1 OR L2) (P) HUMAN
L4	1	S RECOMBINANT HUMAN GELATIN
L5	69	S HUMAN GELATIN
L6	3	S L5 (P) RECOMBINANT
L7	3	DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
L8	16	S RECOMBINANT (A) GELATIN
L9	0	S L8 NOT L1
L10	10	DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L11	0	S L2 (P) HOMOGENEOUS
L12	20	S L2 (P) HYDROXYLAT?
L13	6	DUPLICATE REMOVE L12 (14 DUPLICATES REMOVED)
L14	335	DUPLICATE REMOVE L2 (687 DUPLICATES REMOVED)
L15	3	S L14 (P) ENDOTOXIN

=> s l6 (p) hydroxylat?
L16 0 L6 (P) HYDROXYLAT?

```
=> s bloom strength
L17         57 BLOOM STRENGTH

=> s l6 (p) l17
L18          0 L6 (P) L17

=> s l6 (p) collagen
L19          2 L6 (P) COLLAGEN

=> s (pharmaceutical composition) and l6
L20          0 (PHARMACEUTICAL COMPOSITION) AND L6

=> d his

     (FILE 'HOME' ENTERED AT 10:15:37 ON 08 NOV 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     10:16:01 ON 08 NOV 2002
L1           16 S RECOMBINANT GELATIN
L2         1022 S RECOMBINANT (P) GELATIN
L3          595 S (L1 OR L2 ) (P) HUMAN
L4            1 S RECOMBINANT HUMAN GELATIN
L5           69 S HUMAN GELATIN
L6            3 S L5 (P) RECOMBINANT
L7            3 DUPLICATE REMOVE L6 (0 DUPLICATES REMOVED)
L8           16 S RECOMBINANT (A) GELATIN
L9            0 S L8 NOT L1
L10          10 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)
L11           0 S L2 (P) HOMOGENEOUS
L12          20 S L2 (P) HYDROXYLAT?
L13           6 DUPLICATE REMOVE L12 (14 DUPLICATES REMOVED)
L14         335 DUPLICATE REMOVE L2 (687 DUPLICATES REMOVED)
L15           3 S L14 (P) ENDOTOXIN
L16           0 S L6 (P) HYDROXYLAT?
L17          57 S BLOOM STRENGTH
L18           0 S L6 (P) L17
L19           2 S L6 (P) COLLAGEN
L20           0 S (PHARMACEUTICAL COMPOSITION) AND L6

=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              94.45      94.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                              -9.91      -9.91

STN INTERNATIONAL LOGOFF AT 10:29:43 ON 08 NOV 2002
```